applied microbiology

MDPI

Table S1. Supplemental Studies on Plausible Mechanisms and Relevance for Pro-Argument on Bovine Milk Benefits (Figure 1).

Study	Study Title	Study Abstract Link	Relevance to Benefit-Risk
Kääriö 2016; [1]	Exposure to a farm environment is associated with T helper 1 and regulatory cytokines at age 4.5 years.	https://pubmed.ncbi.nlm.nih.gov/26362849/	This prospective birth cohort study demonstrated additive or synergistic beneficial effects for farming lifestyle and consumption of raw milk associated with enhanced Th1-type immune responses in farm versus non-farm children, repressing allergy-related Th2-type responses. Dose-dependent exposure to farm milk was associated with immune system effects that may contribute to increased tolerance to asthma and allergy protection in children who consume raw milk.
Melnik & Schmitz 2016 [2]	Milk: a postnatal imprinting system stabilizing FoxP3 expression and regulatory T cell differentiation.	https://pubmed.ncbi.nlm.nih.gov/27175277/	This review on beneficial effects of bifidobacteria and lactobacilli summarized evidence from studies on protective effects from both live and heat-killed bacteria, including attenuation of Th2 inflammatory responses, enhancement of anti-inflammatory cytokine IL-10 in 'probiotica-induced anti-inflammatory intestinal immune responses', modulation of Th1/Th2 balance and inducing Tregs. Authors noted that heat-treatment of bacteria may result in loss of immune-regulatory functions.
Von Mutius 2016 [3]	The microbial environment and its influence on asthma prevention in early life.	https://pubmed.ncbi.nlm.nih.gov/26806048/	Overall, this review identified multiple mechanisms involving partly redundant pathways as likely to contribute to asthma protection in diverse microbial environments, controlling for some potential confounding factors including genetics (experimental comparisons between Amish and Hutterite households) and raw milk consumption.
Abbring 2017 [4]	Raw cow's milk prevents the development of airway inflammation in a murine house dust mite-induced asthma model.	https://pubmed.ncbi.nlm.nih.gov/28894452/	This experimental study identified potential mechanisms for the heat-sensitive protective effects of raw milk consumption on induced asthma in mice: reduced local production of pulmonary type 2 cytokines, airway hyper-responsiveness, and pulmonary inflammation.
Boudry 2017 [5]	Bovine milk oligosaccharides decrease gut permeability and improve inflammation and microbial dysbiosis in diet-induced obese mice	http://doi:10.3168/jds.2016-11890	This experimental study identified potential mechanisms in a murine obesity model. The study demonstrated that bovine milk oligosaccharides derived from whey can correct diet-associated microbial dysbiosis (Western diet), reduce gut permeability, and reduce inflammation.
Mezouar 2018 [6]	Microbiome and the immune system: From a healthy steady-state to allergy associated disruption.	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4056765/	This review provides an overview of mechanisms of microbiome-immune system cross talk proposed to influence allergy and asthma risk. Dysbiosis associated with antibiotic-induced susceptibility to pathogens and allergens was associated with dysimmunity, particularly Th2-excessive Treg-deficient states and immune deviations. Research on pathophysiologic checkpoints was hampered by the complexity of interactions, the multiplicity of multifactorial determinants of allergic/atopic diseases, and sparse knowledge of the underlying mechanisms for clinical disease in humans.
Müller-Rompa 2018[7]	An approach to the asthma-protective farm effect by geocoding:	https://pubmed.ncbi.nlm.nih.gov/29314275/	This cohort study (GABRIELA) demonstrated that geocoded distances of residences to farms were negatively correlated with asthma and atopy in children. The associations were related to broader

Study	Study Title	Study Abstract Link	Relevance to Benefit-Risk
	Good farms and better farms.		diversity of microbial exposures for children nearer to farms. The correlation was explained mainly (non-farm children) or partially (farm children) by unprocessed farm milk consumption.
Perdijk 2018[8]	Cow's milk and immune function in the respiratory tract: potential mechanisms.	https://pubmed.ncbi.nlm.nih.gov/29483908/	This review describes homologies between breastmilk and bovine milk and evidence associated with protection against allergies and asthma. Heat sensitive components of raw bovine milk were identified as important drivers not only of allergies and asthma, but also viral infections, fever, and inflammatory conditions in the upper airways. Evidence from epidemiologic and *in vitro*, and *in vivo* studies were presented related to leaky gut and mucosal epithelial barrier function, the microbiota of the gut-lung axis, activity of bovine IgG, and both local mucosal and systemic immunity. Both Toll-like receptors and short chain fatty acids were involved in signaling and cross-talk between the microbiota and immune cells in the gut and respiratory tracts.
Abbring 2019[9]	Raw Cow's Milk Reduces Allergic Symptoms in a Murine Model for Food Allergy—A Potential Role for Epigenetic Modifications	http://doi:10.3390/nu11081721	This experimental study in a mouse animal model demonstrated that feeding of raw cow's milk but not pasteurized milk induced oral tolerance to an unrelated food allergen. Raw milk appears to induce epigenetic effects on FoxP3+ T regulatory cells, resulting in reduced allergic symptoms. Further study is needed to determine if allergy prevention and epigenetic regulation, e.g., histone modification, is caused by specific bioactive components of raw milk.
Frei 2019[10]	Exposure of Children to Rural Lifestyle Factors Associated With Protection Against Allergies Induces an Anti-Neu5Gc Antibody Response	http://doi:10.3389/fimmu.2019.01628	This perspective study documents that the sialic acid Neu5Gc and antibodies produced against it, are associated with consumption of raw cow's milk in farm children and mice. This sialic acid and antibodies against it may function as anti-inflammatory markers and may be useful biomarkers for predicting protection against allergies and asthma.
Butler 2020[11]	Recipe for a Healthy Gut: Intake of Unpasteurised Milk Is Associated with Increased *Lactobacillus* Abundance in the Human Gut Microbiome	http://doi:10.3390/nu12051468	This observational cohort study documented that dietary changes, significantly consumption of raw milk, was associated with changes in gut microbiota, short chain fatty acid levels, richness, and psychobiotic measures of neuroactive potential for raw milk consumers over 12 weeks. Raw milk consumption was associated with increases in abundance of *Lactobacillus* and *Lactococcus* in the gut microbiota. The abundance and predicted functional richness of the gut microbiota and their metabolites may provide an alternative to consuming commercially-produced probiotic supplements to improve physical and mental health, related to microbial cross talk along the gut-brain axis.
Franco-Lopez 2020[12]	Correlations between the Composition of the Bovine Microbiota and Vitamin B12 Abundance.	https://pubmed.ncbi.nlm.nih.gov/32127420/	This experimental study documented that the concentration of the essential vitamin B_{12} in plasma was the strongest predictor of the vitamin in milk. Levels of vitamin in rumen are linked to the absence of vitamin B_{12} consumers (Bacteroidetes) rather than presence of efficient vitamin B_{12} producers (not clearly identified). These data support the theory for an enteromammary pathway of microbial transfer from the GI tract to mammary tissue and milk.

Study	Study Title	Study Abstract Link	Relevance to Benefit-Risk
Hufnafl 2020[13]	Dysbiosis of the gut and lung microbiome has a role in asthma.	https://pubmed.ncbi.nlm.nih.gov/32072252/	Results of this review supported the positive effects of the farming environment (including consumption of raw milk) and the negative effects of allergens, air pollution, antibiotics and other drugs, and indoor air on the microbiota of the GI and respiratory tracts associated with protection against asthma. Dysbiosis of both GI and lung microbiota were linked to increased emergence of asthma.
Quinn 2020[14]	Fraction Rich in Immunoglobulin G Combined with *Bifidobacterium longum* subsp. *infantis* ATCC 15697 Exhibits Synergistic Effects against *Campylobacter jejuni.*	http://doi:10.3390/ijms21134632	This experimental study demonstrated that the combination of two bioactive components of raw bovine milk (*B. infantis* and whey protein) synergistically increased attachment of *B. infantis* to human epithelial cells and increased colonization resistance against the enteropathogen *Campylobacter jejuni*.
Radosavljevic 2020[15]	Digestomics of Cow's Milk: Short Digestion-Resistant Peptides of Casein Form Functional Complexes by Aggregation	http://doi:10.3390/foods9111576	This experimental study demonstrated that simulated gastric digestion of raw milk resulted in aggregation of digested peptides, reaction with human IgE and IgG4 epitopes, and in vivo responses to skin-prick testing in five milk-allergic volunteers. Both raw and pasteurized milks may induce some allergic responses.
van Esch 2020[16]	The Impact of Milk and Its Components on Epigenetic Programming of Immune Function in Early Life and Beyond: Implications for Allergy and Asthma	http://doi:10.3389/fimmu.2020.02141	This review summarized evidence on the effects of human and bovine milk that contribute to epigenetic mechanisms (DNA methylation, histone modification, microRNAs) that modify the expression of human genes. Ingestion of bioactive components of raw human and bovine milks in pregnant women and environmental factors (farming, milk processing, bacterial exposure) were assessed to address the current epidemic of non-communicable and allergic diseases. Many cow milk components demonstrate similar effects on human immune cells as the components of human milk. Some mechanistic pathways appear to explain protection for consumers of raw milks against asthma and allergy via epigenetics.
Wang, Bai, Peng 2020[17]	Fermented milk containing *Lactobacillus casei* Zhang and *Bifidobacterium animalis* ssp. lactis V9 alleviated constipation symptoms through regulation of intestinal microbiota, inflammation, and metabolic pathways	http://doi:10.3168/jds.2020-18639	The experimental portion of this study demonstrated that heat-treated milk (95°C for 5 minutes) supplemented with 4 probiotic strains and incubated at 37°C for 9 hours supported growth of the probiotic strains to high levels. The observational portion of the study documented some mechanistic data for gut microbiota and inflammation that was generated from 26 constipated human volunteers whose symptoms decreased significantly after 28 days of daily consumption of the probiotic fermented milk described above. Three potential mechanisms identified were: fine-tuning gastrointestinal microbiota; fighting inflammation; and regulating metabolic pathways.
Abbring 2021[18]	Raw Milk-Induced Protection against Food Allergic Symptoms in Mice Is Accompanied by Shifts in Microbial Community Structure	http://doi:10.3390/ijms22073417	This experimental study characterized effects of feeding raw or pasteurized milks in a murine model. Mice fed raw or pasteurized milks were subjected to sensitization with ovalbumin. Changes in gut microbiota attributed to raw milk feeding included increased relative abundance of putative butyrate-producers and decreased abundance of putative pro-inflammatory microbes. Raw milk protection in mice was associated with

Study	Study Title	Study Abstract Link	Relevance to Benefit-Risk
			increases in butyrate-producing microbes and decreased putative pro-inflammatory microbes. The addition of alkaline phosphatase to pasteurized milk restored the protective effect of raw milk and mitigated some gut microbiota dysbiosis associated with pasteurized milk. The protective effect of raw cow's milk against ovalbumin-associated food allergy is heat sensitive and is associated with immunological changes including a reduction in allergen specific Th2 cells responsiveness and an increase in Treg activity.

Table S2. Supplemental Studies on Plausible Mechanisms and Relevance for Contra-Argument on Bovine Milk Risks (Figure 1).

Study	Study Title	Study Abstract Link	Relevance to Benefit-Risk
Pricope-Cicolacu 2013[19]	The effect of milk components and storage conditions on the virulence of Listeria monocytogenes as determined by a Caco-2 cell assay.	https://pubmed.ncbi.nlm.nih.gov/23831732/	Results of this *in vitro* experimental study demonstrated that preincubation of human intestinal epithelial Caco-2 cells in raw milk (but not pasteurized milk or buffer) prior to inoculation with *L. monocytogenes*, significantly decreased virulence potential of the pathogen as measured by adhesion, invasion, and intracellular growth. High fat content of pasteurized milk (3.6%) was more protective against listeriosis than lower fat pasteurized milks (1% and 2%). These data are relevant for inclusion in future QMRAs and benefit-risk assessments for raw and pasteurized milks.
McCarthy 2015[20]	The immunological consequences of pasteurisation: Comparison of the response of human intestinally-derived cells to raw versus pasteurised milk.	https://www.sciencedirect.com/science/article/abs/pii/S0958694614001824	This experimental study applied human whole genome microarray analysis of cells exposed to raw or pasteurized milk. Results documented differential expression of 1041 human genes. The 442 genes upregulated by raw milk were associated with immune response, antigen processing and cell surface signaling. The proposed mechanism of protection was increase antigen sampling and presentation via MHC class II molecules, potentially leading to an increase in allergen tolerance. Results suggest an alteration in the immunomodulatory potential of milk following pasteurization. These data are relevant for inclusion in future QMRAs and benefit-risk assessments for raw and pasteurized milks.
Buchanan 2017[21]	A review of *Listeria monocytogenes*: An update on outbreaks, virulence, dose-response, ecology, and risk assessments	http://doi:10.1016/j.foodcont.2016.12.016	This review summarized workshop discussions regarding major scientific advances for QMRAs for listeriosis. One QMRA was the 2003 listeriosis risk assessment by FDA/FSIS that included raw and pasteurized milks. Key advances relevant to updating early QMRAs include: the microbial ecology of growth and survival of pathogens in foods and in competition with healthy gut microbiota; bias in selecting highly virulent outbreak strains for dose-response modeling; and reliance on conservative non-threshold, low-dose linear model forms based on rodent mortality data and adjusted many orders of magnitude for consistency with epidemiologic data. Accounting for deeper knowledge from these and other scientific advances appears likely to reduce the 2003 risk estimates.
Dietert 2017[22]	Safety and risk assessment for the human superorganism	http://doi:10.1080/10807039.2017.1356683	This editorial noted that fundamental misunderstandings human biology rooted in 20th century science causes significant problems with safety and risk assessments that fail to account for the complexities of the human superorganism or holobiont. One misunderstanding regards ingested pathogen doses insufficient to breach the key defense barrier (microimmunosome, including gut microbiota, barrier functions, underlying innate and adaptive immune systems). Dose-response assessments based on 21st century science requires alternatives to the conservative non-threshold model for the frequency and severity of illness. Historical QMRAs have not modeled the microimmunosome as a functional unit or colonization resistance of healthy gut microbiota. The overly simplistic models of salmonellosis were noted as particularly problematic. The evidence on the complexity of microbial ecology

Study	Study Title	Study Abstract Link	Relevance to Benefit-Risk
			of foods, gut microbiota effects including colonization resistance, and sublinear and threshold dose-response models challenge 20th century ideas about evidence-based assessments of safety and risk.
Schröder 2017[23]	A switch in regulatory T cells through farm exposure during immune maturation in childhood.	https://pubmed.ncbi.nlm.nih.gov/27732759/	This longitudinal birth cohort study of 111 children documented significant differential effects of high versus low farm milk consumption on Tregs and their capacity to suppress cytokine secretion, immune markers for asthma. The authors described a counterregulatory mechanism whereby Tregs from asthmatic versus nonasthmatic children increased during maturation to counterbalance exuberant allergic responses. Children in the high farm-milk group had significantly suppressed functional capacity to suppress cytokines relative to rates for low farm-milk children. Effects of farm-milk and animal/stable exposures both contribute to immune maturation of Tregs early during childhood (prior to age 6). These data are relevant for inclusion in future QMRAs and benefit-risk assessments for raw and pasteurized milks.
Coleman 2018[24]	Microbiota and Dose-Response: Evolving Paradigm of Health Triangle	http://doi:10.1111/risa.13121	This symposium paper emphasized case studies where updating assumptions about dose-response assessment for 21st century science following the 'microbiome revolution' dramatically influences risks. An intervention influenced by germ theory and overreliance on antibiotics treatment, intended to reduce the abundance of commensal *S. aureus* in the nasal microbiota of hospital workers, actually increased risk of transmission to patients. Other case studies included: enhanced immunity for elderly volunteers treated with probiotics and prebiotics; and enhanced colonization resistance against salmonellosis in mice when protective gut microbiota are restored, with extension to human salmonellosis. None of the prior QMRAs for raw milk (nor those conducted to date) incorporated such data on the complex interactions of pathogens with the microbiota of foods, gut, and the environment. These data are relevant for inclusion in future QMRAs and benefit-risk assessments for raw and pasteurized milks.
Perdijk 2018[8]	Cow's milk and immune function in the respiratory tract: potential mechanisms.	https://pubmed.ncbi.nlm.nih.gov/29483908/	This review documented homology of breastmilk and bovine milk components and conserved mechanisms contributing to immune homeostasis early in life. Heat sensitive components of raw bovine milk were identified as important drivers of viral infections in the upper airways and fever. Evidence from epidemiologic, *in vitro* and *in vivo* studies were presented related to leaky gut and mucosal epithelial barrier function, the microbiota of the gut-lung axis, activity of bovine IgG, and both local mucosal and systemic immunity. Both Toll-like receptors and short chain fatty acids were involved in signaling and cross-talk between the microbiota and immune cells in the gut and respiratory tracts. These data are relevant for inclusion in future QMRAs and benefit-risk assessments for raw and pasteurized milks.
Benmoussa & Provost 2019[25]	Milk MicroRNAs in Health and Disease	http://doi:10.1111/1541-4337.12424	This review identified a study reporting that numbers of microRNAs in raw milk components were higher than comparable pasteurized components. Although stability of microRNAs may be higher in raw milk, it is uncertain if this effect is linked to health and

Study	Study Title	Study Abstract Link	Relevance to Benefit-Risk
			disease for milk consumers. These data are relevant for inclusion in future QMRAs and benefit-risk assessments for raw and pasteurized milks.
Li 2019[26]	Processing milk causes the formation of protein oxidation products which impair spatial learning and memory in rats.	https://pubs.rsc.org/en/content/articlelanding/2019/ra/c9ra03223a#!divAbstract	This experimental study documented significant adverse effects on spatial learning and memory in rats fed milk processed using heat (boiling, pasteurizing, microwaving, spray drying) and freeze-drying. These results demonstrate the importance to consider risks for pasteurization and other heat treatments (e.g., boiling, spray drying) that may adversely affect human consumers of processed milks. These data are relevant for inclusion in future QMRAs and benefit-risk assessments for raw and pasteurized milks.
Lima 2019[27]	The Bos taurus maternal microbiome: Role in determining the progeny early-life upper respiratory tract microbiome and health.	https://pubmed.ncbi.nlm.nih.gov/30840624/	This experimental study confirms that healthy microbiota of pregnant cows are transferred to offspring, and only one bacterial genus (*Mannheimia*) appeared to be correlated with calf disease. These mechanisms are relevant to consider in microbial benefit risk assessments conducted for raw milk regarding animal and human health.
Melnik & Schmitz 2019[28]	Exosomes of pasteurized milk: potential pathogens of Western diseases	http://doi:10.1186/s12967-018-1760-8	This review provided evidence for potential human adverse effects from dietary exposure to exosomes in pasteurized milks. These data are relevant for inclusion in future QMRAs and benefit-risk assessments for raw and pasteurized milks.
Wu 2019[29]	Rumen fluid, feces, milk, water, feed, airborne dust, and bedding microbiota in dairy farms managed by automatic milking systems.	https://pubmed.ncbi.nlm.nih.gov/30656804/	Results of this experimental study at two dairy farms undermine the assumption that fecal microbiota are the source of bacteria in raw milk. None of the microbial risk assessment conducted to date for raw milk have addressed the complexity of the microbiota of milk and the dairy environment. These data are relevant for inclusion in future QMRAs and benefit-risk assessments for raw and pasteurized milks.

References

1. Kääriö, H.; Huttunen, K.; Karvonen, A.M.; Schaub, B.; von Mutius, E.; Pekkanen, J.; Hirvonen, M.-R.; Roponen, M. Exposure to a Farm Environment Is Associated with T Helper 1 and Regulatory Cytokines at Age 4.5 Years. *Clin. Exp. Allergy J. Br. Soc. Allergy Clin. Immunol.* **2016**, *46*, 71–77, doi:10.1111/cea.12636.
2. Melnik, B.C.; John, S.M.; Carrera-Bastos, P.; Schmitz, G. Milk: A Postnatal Imprinting System Stabilizing FoxP3 Expression and Regulatory T Cell Differentiation. *Clin. Transl. Allergy* **2016**, *6*, 18, doi:10.1186/s13601-016-0108-9.
3. von Mutius, E. The Microbial Environment and Its Influence on Asthma Prevention in Early Life. *J. Allergy Clin. Immunol.* **2016**, *137*, 680–689, doi:10.1016/j.jaci.2015.12.1301.
4. Abbring, S.; Verheijden, K.A.T.; Diks, M.A.P.; Leusink-Muis, A.; Hols, G.; Baars, T.; Garssen, J.; van Esch, B.C.A.M. Raw Cow's Milk Prevents the Development of Airway Inflammation in a Murine House Dust Mite-Induced Asthma Model. *Front. Immunol.* **2017**, *8*, 1045, doi:10.3389/fimmu.2017.01045.
5. Boudry, G.; Hamilton, M.K.; Chichlowski, M.; Wickramasinghe, S.; Barile, D.; Kalanetra, K.M.; Mills, D.A.; Raybould, H.E. Bovine Milk Oligosaccharides Decrease Gut Permeability and Improve Inflammation and Microbial Dysbiosis in Diet-Induced Obese Mice. *J. Dairy Sci.* **2017**, *100*, 2471–2481, doi:10.3168/jds.2016-11890.
6. Mezouar, S.; Chantran, Y.; Michel, J.; Fabre, A.; Dubus, J.-C.; Leone, M.; Sereme, Y.; Mège, J.-L.; Ranque, S.; Desnues, B.; et al. Microbiome and the Immune System: From a Healthy Steady-State to Allergy Associated Disruption. *Hum. Microbiome J.* **2018**, *10*, 11–20, doi:10.1016/j.humic.2018.10.001.
7. Müller-Rompa, S.E.K.; Markevych, I.; Hose, A.J.; Loss, G.; Wouters, I.M.; Genuneit, J.; Braun-Fahrländer, C.; Horak, E.; Boznanski, A.; Heederik, D.; et al. An Approach to the Asthma-Protective Farm Effect by Geocoding: Good Farms and Better Farms. *Pediatr. Allergy Immunol. Off. Publ. Eur. Soc. Pediatr. Allergy Immunol.* **2018**, *29*, 275–282, doi:10.1111/pai.12861.
8. Perdijk, O.; van Splunter, M.; Savelkoul, H.F.J.; Brugman, S.; van Neerven, R.J.J. Cow's Milk and Immune Function in the Respiratory Tract: Potential Mechanisms. *Front. Immunol.* **2018**, *9*, 143, doi:10.3389/fimmu.2018.00143.
9. Abbring, S.; Wolf, J.; Ayechu-Muruzabal, V.; Diks, M.A.P.; Alhamwe, B.A.; Alhamdan, F.; Harb, H.; Renz, H.; Garn, H.; Garssen, J.; et al. Raw Cow's Milk Reduces Allergic Symptoms in a Murine Model for Food Allergy-A Potential Role for Epigenetic Modifications. *Nutrients* **2019**, *11*, E1721, doi:10.3390/nu11081721.

10. Frei, R.; Roduit, C.; Ferstl, R.; O'Mahony, L.; Lauener, R.P. Exposure of Children to Rural Lifestyle Factors Associated with Protection against Allergies Induces an Anti-Neu5Gc Antibody Response. *Front. Immunol.* **2019**, *10*, 1628, doi:10.3389/fimmu.2019.01628.
11. Butler, M.I.; Bastiaanssen, T.F.S.; Long-Smith, C.; Berding, K.; Morkl, S.; Cusack, A.-M.; Strain, C.; Busca, K.; Porteous-Allen, P.; Claesson, M.J.; et al. Recipe for a Healthy Gut: Intake of Unpasteurised Milk Is Associated with Increased Lactobacillus Abundance in the Human Gut Microbiome. *Nutrients* **2020**, *12*, E1468, doi:10.3390/nu12051468.
12. Franco-Lopez, J.; Duplessis, M.; Bui, A.; Reymond, C.; Poisson, W.; Blais, L.; Chong, J.; Gervais, R.; Rico, D.E.; Cue, R.I.; et al. Correlations between the Composition of the Bovine Microbiota and Vitamin B12 Abundance. *mSystems* **2020**, *5*, e00107-20, doi:10.1128/mSystems.00107-20.
13. Hufnagl, K.; Pali-Schöll, I.; Roth-Walter, F.; Jensen-Jarolim, E. Dysbiosis of the Gut and Lung Microbiome Has a Role in Asthma. *Semin. Immunopathol.* **2020**, *42*, 75–93, doi:10.1007/s00281-019-00775-y.
14. Quinn, E.M.; Kilcoyne, M.; Walsh, D.; Joshi, L.; Hickey, R.M. A Whey Fraction Rich in Immunoglobulin G Combined with Bifidobacterium Longum Subsp. Infantis ATCC15697 Exhibits Synergistic Effects against Campylobacter Jejuni. *Int. J. Mol. Sci.* **2020**, *21*, E4632, doi:10.3390/ijms21134632.
15. Radosavljević, J.; Apostolović, D.; Mihailović, J.; Atanasković-Marković, M.; Burazer, L.; van Hage, M.; Ćirković Veličković, T. Digestomics of Cow's Milk: Short Digestion-Resistant Peptides of Casein Form Functional Complexes by Aggregation. *Foods Basel Switz.* **2020**, *9*, E1576, doi:10.3390/foods9111576.
16. van Esch, B.C.A.M.; Porbahaie, M.; Abbring, S.; Garssen, J.; Potaczek, D.P.; Savelkoul, H.F.J.; van Neerven, R.J.J. The Impact of Milk and Its Components on Epigenetic Programming of Immune Function in Early Life and beyond: Implications for Allergy and Asthma. *Front. Immunol.* **2020**, *11*, 2141, doi:10.3389/fimmu.2020.02141.
17. Wang, J.; Bai, X.; Peng, C.; Yu, Z.; Li, B.; Zhang, W.; Sun, Z.; Zhang, H. Fermented Milk Containing Lactobacillus Casei Zhang and Bifidobacterium Animalis Ssp. Lactis V9 Alleviated Constipation Symptoms through Regulation of Intestinal Microbiota, Inflammation, and Metabolic Pathways. *J. Dairy Sci.* **2020**, *103*, 11025–11038, doi:10.3168/jds.2020-18639.
18. Abbring, S.; Engen, P.A.; Naqib, A.; Green, S.J.; Garssen, J.; Keshavarzian, A.; van Esch, B.C.A.M. Raw Milk-Induced Protection against Food Allergic Symptoms in Mice Is Accompanied by Shifts in Microbial Community Structure. *Int. J. Mol. Sci.* **2021**, *22*, 3417, doi:10.3390/ijms22073417.
19. Pricope-Ciolacu, L.; Nicolau, A.I.; Wagner, M.; Rychli, K. The Effect of Milk Components and Storage Conditions on the Virulence of Listeria Monocytogenes as Determined by a Caco-2 Cell Assay. *Int. J. Food Microbiol.* **2013**, *166*, 59–64, doi:10.1016/j.ijfoodmicro.2013.05.027.
20. McCarthy, R.J.; Ross, R.P.; Fitzgerald, G.F.; Stanton, C. The Immunological Consequences of Pasteurisation: Comparison of the Response of Human Intestinally-Derived Cells to Raw versus Pasteurised Milk. *Int. Dairy J.* **2015**, *40*, 67–72, doi:10.1016/j.idairyj.2014.08.019.
21. Buchanan, R.L.; Gorris, L.G.M.; Hayman, M.M.; Jackson, T.C.; Whiting, R.C. A Review of Listeria Monocytogenes : An Update on Outbreaks, Virulence, Dose-Response, Ecology, and Risk Assessments. *Food Control* **2017**, *75*, 1–13, doi:10.1016/j.foodcont.2016.12.016.
22. Dietert, R.R. Safety and Risk Assessment for the Human Superorganism. *Hum. Ecol. Risk Assess. Int. J.* **2017**, *23*, 1819–1829, doi:10.1080/10807039.2017.1356683.
23. Schröder, P.C.; Illi, S.; Casaca, V.I.; Lluis, A.; Böck, A.; Roduit, C.; Depner, M.; Frei, R.; Genuneit, J.; Pfefferle, P.I.; et al. A Switch in Regulatory T Cells through Farm Exposure during Immune Maturation in Childhood. *Allergy* **2017**, *72*, 604–615, doi:10.1111/all.13069.
24. Coleman, M.; Elkins, C.; Gutting, B.; Mongodin, E.; Solano-Aguilar, G.; Walls, I. Microbiota and Dose Response: Evolving Paradigm of Health Triangle. *Risk Anal.* **2018**, *38*, 2013–2028.
25. Benmoussa, A.; Provost, P. Milk MicroRNAs in Health and Disease. *Compr. Rev. Food Sci. Food Saf.* **2019**, *18*, 703–722, doi:10.1111/1541-4337.12424.
26. Li, B.; Mo, L.; Yang, Y.; Zhang, S.; Xu, J.; Ge, Y.; Xu, Y.; Shi, Y.; Le, G. Processing Milk Causes the Formation of Protein Oxidation Products Which Impair Spatial Learning and Memory in Rats. *RSC Adv.* **2019**, *9*, 22161–22175, doi:10.1039/C9RA03223A.
27. Lima, S.F.; Bicalho, M.L. de S.; Bicalho, R.C. The Bos Taurus Maternal Microbiome: Role in Determining the Progeny Early-Life Upper Respiratory Tract Microbiome and Health. *PloS One* **2019**, *14*, e0208014, doi:10.1371/journal.pone.0208014.
28. Melnik, B.C.; Schmitz, G. Exosomes of Pasteurized Milk: Potential Pathogens of Western Diseases. *J. Transl. Med.* **2019**, *17*, 3, doi:10.1186/s12967-018-1760-8.
29. Wu, H.; Nguyen, Q.D.; Tran, T.T.M.; Tang, M.T.; Tsuruta, T.; Nishino, N. Rumen Fluid, Feces, Milk, Water, Feed, Airborne Dust, and Bedding Microbiota in Dairy Farms Managed by Automatic Milking Systems. *Anim. Sci. J. Nihon Chikusan Gakkaiho* **2019**, *90*, 445–452, doi:10.1111/asj.13175.